



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2016-D-1267]

Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act.” For a drug product compounded by an outsourcing facility to qualify for the exemptions under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act), it must not be essentially a copy of one or more approved drug products and must meet the other conditions in section 503B. This guidance sets forth FDA’s policies concerning the “essentially a copy” provision of section 503B.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work to finalize the guidance, submit either electronic or written comments on this draft guidance by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]. Submit comments on information collection issues under the Paperwork

Reduction Act of 1995 by [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <http://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <http://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA-2016-D-1267 for “Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <http://www.regulations.gov> or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <http://www.regulations.gov>. Submit both copies to the Division of

Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at:

<http://www.fda.gov/regulatoryinformation/dockets/default.htm>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <http://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Submit comments on information collection issues to the Office of Management and Budget in the following ways:

- Fax to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, FAX: 202-395-7285, or email to oir_submission@omb.eop.gov. All comments should be identified with the title, “Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act.”

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001

New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Sara Rothman, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 5197, Silver Spring, MD, 301-796-3110.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act.” In 2013, the Drug Quality and Security Act, created a new section 503B of the Act, which describes a new category of compounders called “outsourcing facilities.” Section 503B of the FD&C Act describes the conditions that must be satisfied for human drug products compounded by or under the direct supervision of a licensed pharmacist in an outsourcing facility to qualify for exemptions from the following three sections of the FD&C Act:

- Section 502(f)(1) (21 U.S.C. 352(f)(1)) (concerning labeling of drugs with adequate directions for use);
- Section 505 (21 U.S.C. 355) (concerning the approval of drugs under new drug applications (NDAs) or abbreviated new drug applications (ANDAs)); and
- Section 582 (21 U.S.C. 360eee-1) (concerning drug supply chain security requirements).

One of the conditions that must be met for a compounded drug product to qualify for the exemptions under section 503B of the Act is that “the drug is not essentially a copy of one or more approved drugs” (section 503B(a)(5)).

Section 503B(d)(2) defines “essentially a copy of an approved drug” as:

- A drug that is identical or nearly identical to an approved drug, or a marketed drug not subject to section 503(b) and not subject to approval in an application submitted under section 505, unless, in the case of an approved drug, the drug appears on the drug shortage list in effect under section 506E at the time of compounding, distribution, and dispensing (section 503B(d)(2)(A)); or
- A drug, a component of which is a bulk drug substance that is a component of an approved drug or a marketed drug that is not subject to section 503(b) and not subject to approval in an application submitted under section 505, unless there is a change that produces for an individual patient a clinical difference, as determined by the prescribing practitioner, between the compounded drug and the comparable approved drug (section 503B(d)(2)(B)).

This guidance sets forth FDA’s policies concerning the “essentially a copy” provision of section 503B of the FD&C Act.

This draft guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on the “essentially a copy” provision of section 503B of the FD&C Act. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

Under the Paperwork Reduction Act of 1995 (the PRA) (44 U.S.C. 3501-3520), Federal Agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information that they conduct or sponsor. “Collection of information” is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal Agencies to provide a 60-day notice in the Federal Register concerning each proposed collection of information before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the collection of information associated with this document, FDA invites comments on the following topics: (1) Whether the proposed collection of information is necessary for the proper performance of FDA’s functions, including whether the information will have practical utility; (2) the accuracy of FDA’s estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Under the draft guidance, pursuant to section 503B(d)(2)(B) of the FD&C Act, if an outsourcing facility compounds a drug, the component of which is a bulk drug substance that is a component of an approved drug, there must be a change that produces a clinical difference for an individual patient as determined by the prescribing practitioner. If an outsourcing facility intends

to rely on such a determination to establish that a compounded drug is not essentially a copy of an approved drug, the outsourcing facility should ensure that the determination is documented on the prescription or order (which may be a patient-specific prescription or a non-patient specific order) for the compounded drug.

If a prescription or order does not make clear that the determination required by section 503B(d)(2)(B) has been made, the outsourcing facility may contact the prescriber or healthcare facility, and if the prescriber or healthcare facility confirms it, make a notation on the prescription or order that the prescriber has determined that the compounded product contains a change that produces a clinical difference for patient(s). The date of the conversation with the healthcare facility or prescriber should be included on the prescription or order.

We estimate that annually a total of approximately 40 outsourcing facilities (“number of respondents” in table 1, line 1) will consult a prescriber to determine whether he or she has made a determination that the compounded drug has a change that produces a clinical difference for an individual patient as compared to the comparable approved drug and that outsourcing facilities will document this determination on approximately 4,000 prescriptions or orders for compounded drugs (“total annual disclosures” in table 1, line 1). We estimate that the consultation between the outsourcing facility and the prescriber or health care facility and adding a notation to each prescription or order that does not already document this determination will take approximately 3 minutes per prescription or order.

In addition, if the outsourcing facility compounded a drug that is identical or nearly identical to an approved drug product that appeared on FDA’s drug shortage list, the outsourcing facility should maintain documentation (e.g., a notation on the order for the compounded drug) regarding the status of the drug on FDA’s drug shortage list at the time of compounding,

distribution and dispensing. We estimate that a total of approximately 30 outsourcing facilities (“number of respondents” in table 1, line 2) will document this information on approximately 3,000 prescriptions or orders for compounded drugs (“total annual disclosures” in table 1, line 2). We estimate that checking FDA’s drug shortage list and documenting this information will take approximately 2 minutes per prescription or order.

An outsourcing facility should also maintain records of prescriptions or orders including notations that a prescriber has determined that the compounded drug has a change that produces a clinical difference for an individual patient. Because the time, effort, and financial resources necessary to comply with this collection of information would be incurred by licensed pharmacists and licensed physicians in the normal course of their activities, it is excluded from the definition of “burden” under 5 CFR 1320.3(b)(2).

FDA estimates the burden of this collection of information as follows:

Table 1.--Estimated Annual Third-Party Disclosure Burden¹

Type of Reporting	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
Consultation between the outsourcing facility and prescriber or health care facility, and the notation on the prescription or order documenting the prescriber’s determination of clinical difference.	40	100	4,000	3 minutes	200
Checking FDA’s drug shortage list and documenting on the prescription that the drug is in shortage.	30	100	3,000	2 minutes	100

¹There are no capital costs or operating and maintenance costs associated with this collection of information.

III. Electronic Access

Persons with access to the Internet may obtain the draft guidance at either

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>

or <http://www.regulations.gov>.

Dated: July 6, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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